

### **REMARKS**

Upon entry of the Amendment, claims 40 to 52 are pending in the application. Claims 45 to 48 are withdrawn from consideration. Claims 40, 42, 43 and 49 are amended. Claims 50 to 52 are new.

No new matter is added. The amendment to claim 40 is made to improve the clarity thereof. The amendment to claim 42 corrects a minor clerical error. The specification supports the amendment to claim 43, such as on page 11. The specification supports the amendment to claim 49, such as on page 10. The specification supports new claims 50 to 52, such as on page 10. Entry of the Amendment is respectfully requested.

A power of attorney is being concurrently filed herewith, transferring the power of attorney to the practitioners associated with the customer number 23483. Please also note that the attorney docket number has changed to 2003133.00122.

#### **I. Double Patenting Rejections**

(a) Claims 40, 43 and 49 are rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claim 1 of U.S. Patent No. 6,635,625 (“the ‘625 patent’”); claim 1 of U.S. Patent No. 6,645,482 (“the ‘482 patent’”); claim 1 of U.S. Patent No. 6,624,148 (“the ‘148 patent’”); claim 1 of U.S. Patent No. 6,641,806 (“the ‘806 patent’”); claims 1 to 13 of U.S. Patent No. 6,984,667 (“the ‘667 patent’”); and claims 1 and 2 of U.S. Patent No. 7,115,278 (“the ‘278 patent’”); in view of Widyarini *et al.* (“Widyarini”) and U.S. Pub. App. No. 2002/0028779 to High *et al.* (“High ‘779’”).

Further, claims 41, 42, and 44 are rejected on the ground of nonstatutory obviousness-type double patenting rejection as allegedly being unpatentable over claim 1 of the ‘625 patent, in view of Widyarini and High ‘779, in further view of Ip *et al.* (“Ip”).

Applicant respectfully traverses these rejections.

Referring to page 3 of the Office Action, the Examiner asserts a person of ordinary skill in the art would have incorporated an isoflavonoid to each of the compositions of the '625 patent, the '482 patent, the '148 patent, the '806 patent, the '667 patent, and the '278 patent. Widyarini discloses that isoflavones derived from many edible plants have been reported to possess significant antioxidant, estrogenic and tyrosine kinase inhibitory activity. *See* Abstract. Widyarini discloses that the isoflavone genistein has provided protective effects against the pathology of UV irradiation. *See* p. 465, right column, lines 16 to 19.

Further, High '779 discloses that genistein is a tyrosine kinase inhibitor. *See* paragraph [0041]. High '779 discloses that its tyrosine kinase inhibitor treats a neuropathological state, such as persistent pain, arthritis, ulcerative colitis, inflammatory bowel disease, Crohn's disease, pancreatitis, asthma, stroke, brain injury, spinal cord injury, epileptogenesis, or viral invasion.

Rejection of a patent on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support a legal conclusion of obviousness. *KSR International v. Teleflex*, 127 S. Ct. 1727, 1741 (2007).

A person of ordinary skill in the art would not have incorporated an isoflavone to the compositions of the '625 patent, the '482 patent, the '148 patent, the '806 patent, the '667 patent, and the '278 patent. The disclosure in Widyarini that isoflavones may possess antioxidant, estrogenic and tyrosine kinase inhibitory activity is not sufficiently specific to provide a reason to incorporate the isoflavone. High '779 reinforces this vagueness, as it discloses that its tyrosine kinase inhibitor treats a wide variety of physical conditions. Moreover, the treatment of UV pathology, as disclosed in Widyarini, is not a treatment provided by the compositions of the '625 patent, the '482 patent, the '148 patent, the '806 patent, the '667 patent, and the '278 patent. No specific reason has been identified to demonstrate that a person of ordinary skill in the art would have selected the isoflavone disclosed in Widyarini or High '779 to incorporate into the

compositions of the '625 patent, the '482 patent, the '148 patent, the '806 patent, the '667 patent, and the '278 patent.

Further, treatment of inflammatory activity, by itself, is not a sufficient reason to incorporate the isoflavonoids disclosed in Widyarini and High '779. Cancer inflammation is not the same as the inflammation present in, for example, arthritis. A mast cell may secrete inflammatory anti-tumor molecules or inflammatory pro-tumor molecules. Examples of the inflammatory anti-tumor molecule include tumor necrosis factor (TNF), interleukin-1, interleukin 4 and interleukin-6. By contrast, examples of inflammatory pro-tumor molecules include vascular endothelial growth factor (VEGF), heparin, histamine, platelet-derived growth factor (PDGF), nerve GF (NGF) and stem-cell factor (SCF). When the mast cell penetrates a tumor, for example, the mast cell does not release TNF, but secretes VEGF. The secretion of VEGF results in neovascularization (neoangiogenesis) and permits tumor nourishment. It follows that the random selection of anti-inflammatory treatments may result in nourishing a tumor, instead of treating the tumor. As such, the treatment of inflammation, by itself, does not clarify whether the treatment is directed at TNF or VEGF.

(b) Claims 40, 43 and 49 are *provisionally* rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claim 40 of copending Application No. 10/610909 in view of Widyarini and High '667.

As the rejection is provisional, Applicant defers response to the rejection.

## **II. Claim Rejections – 35 U.S.C. § 112**

Claims 40 to 44 and 49 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

Referring to pages 5 to 6 of the Office Action, the Examiner asserts that claims 40 and 42 are indefinite. The Examiner asserts that the term “heavily” in claim 40 is indefinite. The Examiner asserts that “said chemotherapeutic agent” in claim 42 has no antecedent basis.

Claims 40 and 42 are amended to address the issues raised by the Examiner.

### **III. Claim Rejections – 35 U.S.C. § 103**

Claims 41, 42 and 44 are rejected under 35 U.S.C. § 103, as allegedly being unpatentable over WO 97/21434 to Florio (“Florio ‘434’”), in view of U.S. Patent No. 5858371 to Singh *et al.* (“Singh ‘371’”), U.S. Patent No. 4,265,823 to Nobile *et al.* (“Nobile ‘823’”), Widyarini and High ‘779.

Further, claims 41, 42, and 44 are rejected under 35 U.S.C. § 103, as allegedly being unpatentable over Florio ‘434, in view of Singh ‘371, Nobile ‘823, Widyarini, High ‘779, in further view of Ip.

Referring to pages 6 to 7 of the Office Action, the Examiner concedes that Florio ‘434 fails to teach quercetin, olive kernel extract, and isoflavonoids. The Examiner attempts to cure this deficiency by looking to Singh ‘371, Nobile ‘823, Widyarini, High ‘779, and Ip. Singh ‘371 discloses that the composition thereof includes a pharmaceutically acceptable carrier and a mixture of flavonoids. *See* col. 2, lines 43-52. Nobile discloses that the aurothiomalate-estrogenic compounds thereof possess anti-inflammatory and estrogenic activity for the treatment of rheumatoid arthritis and menopausal and other conditions related to estrogen deficiency. *See* col. 10, lines 20-37. Widyarini discloses that isoflavones derived from many edible plants have been reported to possess significant antioxidant, estrogenic and tyrosine kinase inhibitory activity. *See* Abstract. High ‘779 discloses that genistein is a tyrosine kinase inhibitor. *See* paragraph [0041]. Ip discloses that treatment of rats with tamoxifen resulted in marked suppression of tumor growth in 91 % of the tumors examined. *See* Abstract.

Rejection of a patent on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support a legal conclusion of obviousness. *KSR International v. Teleflex*, 127 S. Ct. 1727, 1741 (2007).

At a minimum, a person of ordinary skill in the art would not have combined Florio '434, with Widyarini and/or High '779. Florio '434 discloses that its combination of nutritional supplements provides symptomatic relief from arthritis. *See* Abstract. As described above, Widyarini discloses that the isoflavone genistein has provided protective effects against the pathology of UV irradiation. *See* p. 465, right column, lines 16 to 19. High '779 discloses that its tyrosine kinase inhibitor treats a neuropathological state, such as persistent pain, arthritis, ulcerative colitis, inflammatory bowel disease, Crohn's disease, pancreatitis, asthma, stroke, brain injury, spinal cord injury, epileptogenesis, or viral invasion.

The disclosure in Widyarini that isoflavones may possess antioxidant, estrogenic and tyrosine kinase inhibitory activity is not sufficiently specific to provide a reason to incorporate the isoflavone. High '779 reinforces this vagueness, as it discloses that its tyrosine kinase inhibitor treats a wide variety of physical conditions. No reason has been provided to indicate that person of ordinary skill in the art would have selected arthritis, as disclosed in Florio '434 from the wide range of conditions which the tyrosine kinase inhibitor disclosed in High '779 would treat. As such, no specific reason has been identified to demonstrate that a person of ordinary skill in the art would have selected the isoflavone disclosed in Widyarini or High '779 to add to the nutritional supplements disclosed in Florio '434.

Further, Singh '371 discloses the composition thereof treats anorectal diseases including hemorrhoids and colonic diseases. *See* Abstract. No reason has been identified which would explain why a person of ordinary skill in the art would combine the composition disclosed in Singh '371, which treats anorectal diseases, with the combination of nutritional supplements that provide symptomatic relief from arthritis.

As described above, the treatment of inflammatory activity, by itself, is not a sufficient reason to combine the chondroitin sulfate disclosed in Florio '434 with the flavonoids disclosed in Singh '371 or the isoflavone disclosed in Widyarini or High '779. Cancer inflammation is not the same as the inflammation present in, for example, arthritis. A mast cell may secrete inflammatory

anti-tumor molecules or inflammatory pro-tumor molecules. Examples of the inflammatory anti-tumor molecule include tumor necrosis factor (TNF), interleukin-1, interleukin 4 and interleukin-6. By contrast, examples of inflammatory pro-tumor molecules include vascular endothelial growth factor (VEGF), heparin, histamine, platelet-derived growth factor (PDGF), nerve growth factor (NGF) and stem-cell factor (SCF). When the mast cell penetrates a tumor, for example, the mast cell does not release TNF, but secretes VEGF. The secretion of VEGF results in neovascularization (neoangiogenesis) and permits tumor nourishment. It follows that the random selection of anti-inflammatory treatments may result in nourishing a tumor, instead of treating the tumor. As such, the treatment of inflammation, by itself, does not clarify whether the treatment is directed at TNF or VEGF.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Applicant herewith petitions the Director of the USPTO to extend the time for reply to the above-identified Office Action for an appropriate length of time, if necessary. Any fee due under 37 C.F.R. § 1.17(a) is being paid via the USPTO Electronic Filing System, or if not paid through EFS, please charge our Deposit Account No. 08-0219, under Order No. 2003133.00122 from which the undersigned is authorized to draw.

Respectfully submitted,

Dated: June 30, 2008

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